

CLAIMS

1. The use of an inhibitor of a neuropeptide Y (NPY), which inhibitor when in use is selective for an NPY associated with male genitalia, in the preparation of a medicament for the treatment or prevention of male erectile dysfunction (MED).
2. The use of an inhibitor of neuropeptide Y Y1 receptor (NPY Y1), which inhibitor when in use is selective for an NPY Y1 associated with male genitalia, in the preparation of a medicament for the treatment or prevention of MED.
3. The use according to claim 1 or claim 2, wherein said inhibitor when in use is highly selective for NPY/NPY Y1 located in male genitalia.
4. The use according to any one of claims 1-3, wherein said inhibitor has no, or substantially no, activity towards endopeptidase NEP and/or angiotensin converting enzyme.
5. The use according to any one of the preceding claims wherein said treatment or prevention of MED is selective.
6. The use according to any one of the preceding claims wherein an increase in intracavernosal pressure is observed.
7. The use according to any one of the preceding claims wherein the medicament is administered by mouth.
8. The use according to any one of the preceding claims wherein said inhibitor is when in use highly selective for NPY and/or NPY Y1 receptors associated with the corpus cavernosum.
9. The use according to any one of the preceding claims, wherein said NPY and/or NPY Y1 inhibitor is administered before and/or during sexual arousal.
10. The use of an NPY Y1 inhibitor in the manufacture of a medicament for selectively increasing the intracavernosal pressure during sexual arousal.

11. A pharmaceutical composition for use in the treatment of male erectile dysfunction (MED); the pharmaceutical composition comprising an inhibitor of a neuropeptide Y (NPY), which inhibitor when in use is selective for an NPY associated with male genitalia; wherein the inhibitor is optionally admixed with a pharmaceutically acceptable carrier, diluent or excipient.
12. A pharmaceutical composition according to claim 10 wherein the inhibitor is an inhibitor of NPY Y1.
13. A method of treating or preventing MED in a human or animal which method comprises administering to an individual an effective amount of an NPYi, which NPYi when in use is selective for an NPY associated with male genitalia, wherein the NPYi, is optionally admixed with a pharmaceutically acceptable carrier, diluent or excipient.
14. A method according to claim 13 wherein the inhibitor is an NPY Y1 inhibitor.
15. A method of treating or preventing MED in a human or animal which method comprises delivering to an individual an NPYi that is capable of selectively increasing the intracavernosal pressure during sexual arousal.
16. A method according to claim 15 wherein said NPYi is NPY Y1i.
17. An assay method for identifying an agent that can be used to treat MED, the assay comprising: determining whether a test agent can directly enhance the endogenous erectile process; wherein said enhancement is defined as a potentiation of intracavernosal pressure (and/or cavernosal blood flow) in the presence of a test agent; such potentiation by a test agent is indicative that the test agent may be useful in the treatment of MED and wherein said test agent is an NPYi.
18. An assay according to claim 17 wherein said test agent is an NPY Y1.

19. An assay according to claim 17 or claim 18 wherein said test agent selectively inhibits NPY or NPY Y1 receptors associated with the genitalia.
20. A process comprising the steps of:
  - 5 (a) performing an assay according to any one of claims 17-19;
  - (b) identifying one or more agents capable of inhibiting NPY or NPY Y1; and
  - (c) preparing a quantity of those one or more identified agents; and wherein said agent is a NPYi or an NPY Y1i.
- 10 21. A process according to claim 20 wherein said process further comprises testing said one or more agents identified in step (b) for their effect on arterial blood pressure and selecting agents with no, or substantially no, effect on blood pressure.
- 15 22. An assay method for identifying an agent that can be used to treat or prevent MED, the assay comprising: contacting a test agent which has a moiety capable of inhibiting the metabolic breakdown of a peptide (preferably a fluorescent labelled peptide), said peptide being normally metabolised by NPY or NPY Y1; and measuring the activity and/or levels of peptide remaining after
  - 20 a fixed time (for example via fluorometric analysis); wherein the change in the level of the peptide measured by fluorescence is indicative of the potency (IC50) of the test agent and is indicative that the test agent may be useful in the treatment of MED; and wherein said test agent is an NPYi.
- 25 23. An assay according to claim 22 wherein said test agent is an NPY Y1.
24. A method of treating MED with an agent; wherein the agent is capable of inhibiting NPY or NPY Y1 in an *in vitro* assay method; wherein the *in vitro* assay method is the assay method defined in any one of claims 22-23.
- 30 25. An agent identified by the assay methods according to claims 17-19 or claims 22-23.
26. An agent according to claim 25 for use in treating or preventing MED.

27. A medicament for oral administration to treat MED, wherein the medicament comprises the agent according to claim 25.
28. A diagnostic method wherein the method comprises: isolating a sample from a male; determining whether the sample contains an entity present in such an amount as to cause MED; wherein the entity has a direct effect on the endogenous erectile process in the corpus cavernosum of the male; and wherein said entity can be modulated to achieve a beneficial effect by use of an agent, and wherein said agent is an NPYi or an NPY Y1i.
29. A diagnostic composition or kit comprising means for detecting an entity in an isolated male sample; wherein the means can be used to determine whether the sample contains the entity and in such an amount to cause MED, or is in an amount so as to cause MED; wherein the entity has a direct effect on the endogenous erectile process and wherein said entity can be modulated to achieve a beneficial effect by use of an agent; and wherein said agent is an NPYi or an NPY Y1i.
30. An animal model for identifying agent capable of treating MED, said model comprising an anaesthetised animal including means to measure changes in intracavernosal pressure and/or cavernosal blood flow of said animal following stimulation of the pelvic nerve thereof; and wherein said agent is an NPYi or an NPY Y1i.
31. An animal model according to claim 30 wherein said model further comprising means to measure arterial blood pressure of said animal.
32. An assay method for identifying an agent that can directly enhance the endogenous erectile process in order to treat MED, the assay method comprising: administering an agent to the animal model of claim 30 or claim 31; and measuring the change in the endogenous erectile process; wherein said change is defined as a potentiation of intracavernosal pressure (and/or cavernosal blood flow) in the animal model in the presence of a test agent as defined; and wherein said agent is an NPYi or an NPY Y1i.

33. The use according to any one of claims 1-10, wherein in addition to the treatment of MED, abnormal drink and food intake disorders, in particular obesity, anorexia, bulimia and metabolic disorders are also treated.
- 5 34. The use of a combination consisting of one or more NPYi's and one of the following auxiliary active agents in the manufacture/preparation of a medicament for the treatment or prevention of MED:
- 10 (i) Naturally occurring or synthetic prostaglandins or esters thereof.;
  - (ii)  $\alpha$  - adrenergic receptor antagonist compounds;
  - (iii) NO-donor (NO-agonist) compounds;
  - (iv) Potassium channel openers or modulators;
  - 15 (v) Dopaminergic agents, preferably apomorphine or a selective D2, D3 or D2/D<sub>3</sub>agonist;
  - (vi) Vasodilator agents;
  - (vii) Thromboxane A<sub>2</sub> agonists;
  - (viii) CNS active agents;
  - (ix) Ergot alkaloids;
  - 20 (x) Compounds which modulate the action of natruretic factors in particular atrial naturetic factor (also known as atrial naturetic peptide), B type and C type naturetic factors such as inhibitors or neutral endopeptidase;
  - (xi) Angiotensin receptor antagonists such as losartan;
  - 25 (xii) Substrates for NO-synthase, such as L-arginine;
  - (xiii) Calcium channel blockers such as amlodipine;
  - (xiv) Antagonists of endothelin receptors and inhibitors or endothelin-converting enzyme;
  - (xv) Cholesterol lowering agents such as statins (e.g. atorvastatin/ Lipitor- trade mark) and fibrates;
  - 30 (xvi) Antiplatelet and antithrombotic agents, e.g. tPA, uPA, warfarin, hirudin and other thrombin inhibitors, heparin, thromboplastin activating factor inhibitors;
  - (xvii) Insulin sensitising agents such as rezulin and hypoglycaemic agents such as glipizide;
  - 35 (xviii) L-DOPA or carbidopa;

- (xix) Acetylcholinesterase inhibitors such as donezipil;
- (xx) Steroidal or non-steroidal anti-inflammatory agents;
- (xxi) Estrogen receptor modulators and/or estrogen agonists and/or estrogen antagonists;
- 5 (xxii) A PDE inhibitor, more particularly a PDE 2, 3, 4, 5, 7 or 8 inhibitor, preferably PDE2 or PDE5 inhibitor and most preferably a PDE5 inhibitor;
- (xxiii) An NEP inhibitor;
- (xxiv) Vasoactive intestinal protein (VIP), VIP mimetic, VIP analogue,  
10 more particularly mediated by one or more of the VIP receptor subtypes VPAC1, VPAC or PACAP (pituitary adenylate cyclase activating peptide), one or more of a VIP receptor agonist or a VIP analogue or a VIP fragment, one or more of a  $\alpha$ -adrenoceptor antagonist with VIP combination;
- 15 (xxv) A melanocortin receptor agonist or modulator or melanocortin enhancer;
- (xxvi) A serotonin receptor agonist, antagonist or modulator, more particularly agonists, antagonists or modulators for 5HT1A (including VML 670), 5HT2A, 5HT2C, 5HT3 and/or 5HT6  
20 receptors;
- (xxvii) A testosterone replacement agent (including dehydroandrostendione), testosterone (Tostrelle), dihydrotestosterone or a testosterone implant;
- (xxviii) Estrogen, estrogen and medroxyprogesterone or  
25 medroxyprogesterone acetate (MPA) (i.e. as a combination), or estrogen and methyl testosterone hormone replacement therapy agent;
- (xxix) A modulator of transporters for noradrenaline, dopamine and/or serotonin;
- 30 (xxx) A purinergic receptor agonist and/or modulator;
- (xxxi) A neurokinin (NK) receptor antagonist;
- (xxxii) An opioid receptor agonist, antagonist or modulator, preferably agonists for the ORL-1 receptor;
- (xxxiii) An agonist or modulator for oxytocin/vasopressin receptors,  
35 preferably a selective oxytocin agonist or modulator;
- (xxxiv) Modulators of cannabinoid receptors;

(xxxv) A bombesin receptor antagonist, more particularly a bombesin BB<sub>1</sub>, BB<sub>2</sub>, BB<sub>3</sub>, or BB<sub>4</sub> receptor antagonist, preferably a bombesin BB<sub>1</sub> inhibitor;

(xxxvi) A SEP inhibitor;

5 (xxxvii) An agent capable of modulating the activity of an intermediate conductance calcium-activated potassium (IK<sub>Ca</sub>) channel in the sexual genitalia of an individual.

10 35. The use of a combination consisting of one or more NPYi's and one or more PDEi's in the manufacture/preparation of a medicament for the treatment or prevention of MED.

36. The use according to claim 35 wherein said NPYi is an NPY Y1i.

15 37. The use according to claim 35 or claim 36 wherein said PDEi is a PDE5i.

38. The use according to any one of claims 35-37 wherein the medicament is administered by mouth.

20 39. A pharmaceutical composition consisting of one or more NPYi's and one or more PDEi's, optionally admixed with a pharmaceutically acceptable carrier, diluent or excipient.

25 40. A pharmaceutical composition according to claim 39 wherein said NPYi is a NPY Y1i.

41. A pharmaceutical composition according to claims 39 or 40 wherein said NPY Y1i is highly selective for NPY Y1 receptors associated with genitalia.

30 42. A pharmaceutical composition according to claim 39 or claim 41 wherein said PDEi is a PDE5i.

43. A pharmaceutical composition according to any one of claims 39 to 42 wherein the composition is administered by mouth.

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